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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/797,366	03/09/2004	Avi Ashkenazi	39780-1618P2C1-1	5045

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EXAMINER	
SAOUD, CHRISTINE J	
ART UNIT	PAPER NUMBER
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/797,366	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Christine J. Saoud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Claims 1-38 have been canceled and claims 39-45 have been added as requested in the preliminary amendment of 28 June 2006. Claims 39-45 are pending in the instant application.

Priority

According to the priority statement of 28 June 2006, it appears that the claimed subject matter defined in the instant application is supported by PCT application PCT/US00/04414 filed 2/22/2000. Based on the invention given by Applicant and an inspection of the patent applications, the Examiner has concluded that the subject matter defined in this application is supported by the disclosure PCT/US00/04414, filed 2/22/2000 but is not supported by any of the other applications because the claimed subject matter does not have utility/enablement. The use of the claimed invention for inhibition of VEGF stimulated proliferation of adrenal cortical capillary endothelial cells is first taught in PCT/US00/04414, and this is found to have utility and is enabled by the specification as filed. Accordingly, the subject matter defined in claims 39-45 has an effective filing date of 2/22/2000.

Should the Applicant disagree with the Examiner's factual determination above, it is incumbent upon the Applicant to provide the serial number and specific page number(s) of any parent application filed prior to 2/22/2000 which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims

which Applicant considers to have been in possession of and fully enabled for prior to 2/22/2000.

The claims recite that the polypeptide is capable of inducing c-fos in endothelial cells. However, the specification does not teach that the polypeptide of SEQ ID NO:4 has this activity (see page 215 of the specification). Furthermore, this biological activity does not support utility/enablement for the claimed invention and therefore, priority cannot be granted based on the recitation of this activity.

The state of the art indicates that c-fos is a subunit of AP-1, which plays a large number of diverse roles in physiological processes, and is greatly affected by many stimuli, cell types, and cellular environments (see Hess et al., 2004, J. Cell Science 117:5965-5973). For example, homocysteine induces c-fos expression, which sometimes results in mitogenesis, and sometimes does not (Suzuki et al., 2000, Free Radical Biol. and Med. 28:39-45; esp. p. 44, right hand column, second paragraph). Finally, c-fos also plays varying roles in tumorigenesis, including apparently opposite roles (Milde-Langosch, 2005, Eur. J. Cancer 41:2449-2461).

Due to the large quantity of experimentation necessary to determine how to use the claimed genus of polypeptides, the lack of direction/guidance presented in the specification regarding such polypeptides, the absence of working examples directed to the polypeptides, the complex nature of the invention, the contradictory state of the prior art, the unpredictability of the effects of c-fos expression, and the breadth of the claims, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention. Because the claimed invention does not meet the requirements of

112/1st paragraph for these reasons, priority cannot be granted based on this assay.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See page 124, line 37. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Several of the pages of the specification have large blank portions (see at least page 95 and 90). Additionally, pages 78-98 are directed to Tables that have formatting problems (lines wrap to include characters on empty lines). Table 7 at pages 219-222 includes the Table heading in the middle of the page, suggesting that the pagination is off. The entire specification should be reviewed for proper formatting and appropriate correction is required.

If Applicant chooses to correct these deficiencies by submission of a substitute specification, please note the following.

> A substitute specification must not contain new matter. The substitute specification must be submitted with markings showing all the changes relative to the immediate prior version of the specification of record (including changes made to the first paragraph for claims of priority to earlier filed applications). The text of any added subject matter must be shown by underlining the added text. The text of any deleted matter must be shown by strike-through except that double brackets placed before and after the deleted characters may be used to show deletion of five or fewer consecutive characters. The text of any deleted subject matter must be shown by being placed within double brackets if strike-through cannot be easily perceived. An accompanying clean version (without markings) and a statement that the substitute specification contains no new matter must also be supplied. Numbering the paragraphs of the specification of record is not

considered a change that must be shown.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are directed to polypeptides of SEQ ID NO:4 and include the limitation "wherein said polypeptide is capable of inducing c-fos in endothelial cells. The instant specification calls the protein of SEQ ID NO:4, PRO217. Example 84 of the specification (at pages 214-215) describes Assay 34 which tests the ability of a protein to induce c-fos in endothelial cells. The only PRO polypeptide which tested positive in this ass is PRO287. Therefore, the instant specification does not provide support for a polypeptide of SEQ ID NO:4(PRO217) which has the ability to induce c-fos in endothelial cells. The claims are considered new matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 39-40, 42, 44-45 are rejected under 35 U.S.C. 102(a) as being anticipated by HSIEH et al. (Nature 398: 431-436, 1999).

HSIEH et al. disclose an isolated polypeptide which has 99.7% amino acid sequence identity to the amino acid sequence of the polypeptide shown in Figure 4 (SEQ ID NO:4). See Figure 1. HSIEH et al. further disclose a chimeric molecule, including a fusion with an IgG heavy-chain (see paragraph 7). Therefore, the claims are anticipated by the prior art.

Claims 39-45 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over HSIEH et al. (Nature 398: 431-436, 1999).

The disclosure of HSIEH et al. is as described above. The single difference in amino acid sequence between the polypeptide of SEQ ID NO:4 recited in the instant claims and the polypeptide of HSIEH et al. occurs at position 178. Specifically, the amino acid at position 178 in SEQ ID NO:4 of the instant application is glutamine, whereas the amino acid at position 178 of HSIEH et al. is leucine.

The courts have long recognized that sequencing errors can occur (*Ex parte Maizel*; 27 USPQ2d 1662, BPAI 1992, see especially pp. 1663 and 1666). The instant

specification also recognizes that the sequences disclosed in the sequence listing may not be exact. In the instant specification, it is stated that:

> "for the PRO polypeptides and encoding nucleic acids described herein, Applicants have identified what is believed to be the reading frame best identifiable with the sequence information available at the time."

Therefore, it is reasonable to expect that the single amino acid difference at position 178 of SEQ ID NO:4 of the instant application and the protein of HSIEH et al. may be the result of a sequencing error, and that the actual clones of the instant application and HSIEH et al., in fact, have identical sequences.

The Examiner is unable to determine whether the prior art disclosure actually possesses the characteristic of the sequence of SEQ ID NO:4. With these conditions, where the product seems to be identical, then the burden shifts to Applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention. Note the case law of *In re Best* 195 USPQ 430, 433 (CCPA 1977).

Claims 39-40, 42, 44-45 are rejected under 35 U.S.C. 102(b) as being anticipated by BREWER et al. (WO 98/54963; published 10 December 1998).

BREWER et al. teach a polypeptide (SEQ ID NO:426) which has approximately 99% amino acid sequence identity with the claimed polypeptide of SEQ ID NO:4. See attached sequence alignment which references claim 11 and pages 579-580. The reference is 772 pages in length, and therefore, will not be provided in this Office action unless Applicant specifically requests the entire document. BREWER et al. further

disclose a chimeric molecule, including a fusion with an IgG heavy-chain (see page 236).

Claims 39-45 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over BREWER et al. (WO 98/54963; published 10 December 1998).

BREWER et al. teach a polypeptide (SEQ ID NO:426) which has approximately 99% amino acid sequence identity with the claimed polypeptide of SEQ ID NO:4. See attached sequence alignment which references claim 11 and pages 579-580. The differences between the claimed polypeptide and the polypeptide of BREWER et al. are found at positions 264, 300 and 380. Positions 264 and 300 are indicated to be Xaa, which is a wildcard amino acid. Frequently in the biotech. arts, amino acid sequence analysis fails to reliably provide each and every amino acid in a protein sequence. This is sometimes due to disulfide bonds between cysteine residues. Therefore, the amino acids at these positions may very well be cysteine residues (inherent to the polypeptide of BREWER et al), which would anticipate the instant claims since the residues at these positions in SEQ ID NO:4 are cysteine residues. With regard to inherency, where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, *the applicant has the burden of showing that they are not* (emphasis added)." *In re Spada*, 15 USPQ2d 1655,

1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 195 USPQ 430, 433 (CCPA 1977). In re Papesch, 315 F.2d 381, 137 USPQ 42, 51 (CCPA 1963) held that "From the standpoint of patent law, a compound and all its properties are inseparable."

In the alternative, it would have been *prima facie* obvious for one of ordinary skill in the art to place any one of the known amino acids in the recited positions of BREWER et al. since these positions were indicated to be Xaa, which could be any amino acid. The number of embodiments is relatively small, considering only two positions are indicated and it would be well within the skill of the artisan to substitute these two positions and isolate the encoded protein. It is noted that the protein of BREWER et al. has an extra amino acid at position 380, however, the instant claims recite "comprising", which encompasses additional amino acids.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine J. Saoud whose telephone number is 571-272-0891. The examiner can normally be reached on Monday-Friday, 6AM-2PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CHRISTINE J. SAOUD
PRIMARY EXAMINER
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